

Clai

[illegible]

Fig. 1

```
1 GCAGTAACTCCTTCCGTAATTGATAACATACCTTTCTAAAATTGAAAATGAATATG
1▶AlaVal Thr ProSer Val IleAspAsnIleLeuSer LysIleGluAsnGluTyr G
EcoNI (72)
56 AGGTTTTATATTTTAAACCTTTAGCAGGTGTTTATAGAAGTTTAAAAACAATT
19▶IuValLeuTyrLeuLysProLeuAlaGlyValTyrArgSerLeuLysLysGlnLe
111 AGAAAATAACGTTATGACATTTAATGTTAATGTTAAGGATATTTTAAATTCACGA
37▶uGluAsnAsnValMetThrPheAsnValAsnValLysAspIleLeuAsnSerArg
166 TTTAATAAACGTGAAAATTTCAAAAATGTTTAGAATCAGATTTAATTCATATA
56▶PheAsnLysArgGluAsnPheLysAsnValLeuGluSerAspLeuIleProTyrL
221 AAGATTTAACATCAAGTAATTATGTTGTCAAAGATCCATATAAATTTCTTAATAA
74▶ysAspLeuThrSerSerAsnTyrValValLysAspProTyrLysPheLeuAsnLy
276 AGAAAAAGAGATAAATTCCTTAAGCAGTTATAATTATATTAAGGATTCATAGAT
92▶sGluLysArgAspLysPheLeuSerSerTyrAsnTyrIleLysAspSerIleAsp
331 ACGGATATAAATTTTGCAAAATGATGTTCTTGGATATTATAAATATTATCCGAAA
111▶ThrAspIleAsnPheAlaAsnAspValLeuGlyTyrTyrLysIleLeuSerGluL
386 AATATAAATCAGATTTAGATTTCAATTAAAAAATATATCAACGACAAACAAGTGA
129▶ysTyrLysSerAspLeuAspSerIleLysLysTyrIleAsnAspLysGlnGlyGly
441 AAATGAGAAATACCTTCCCTTTTAAACAATATTGAGACCTTATATAAACAGTT
147▶uAsnGluLysTyrLeuProPheLeuAsnAsnIleGluThrLeuTyrLysThrVal
496 AATGATAAAATGATTTATTTGTAATTCATTAGAAGCAAAAGTTCTAAATTTATA
166▶AsnAspLysIleAspLeuPheValIleHisLeuGluAlaLysValLeuAsnTyrT
551 CATATGAGAAATCAAAACGTAGAGTTAAAATAAAAGAACTTAATTACTTAAAAAC
184▶hrTyrGluLysSerAsnValGluValLysIleLysGluLeuAsnTyrLeuLysTh
606 AATTCAAGACAAATTGGCAGATTTTAAAAAATAACAATTTTCGTTGGAATTGCT
202▶rIleGlnAspLysLeuAlaAspPheLysLysAsnAsnAsnPheValGlyIleAla
661 GATTTATCAACAGATTATAACCATAATACTTATTGACAAAGTTCCCTAGTACAG
221▶AspLeuSerThrAspTyrAsnHisAsnAsnLeuLeuThrLysPheLeuSerThrG
716 GTATGGTTTTTGAAAATCTTGCTAAAACCGTTTTATCTAATTTACTTGATGGAAA
239▶IyMetValPheGluAsnLeuAlaLysThrValLeuSerAsnLeuLeuAspGlyAs
771 CTTGCAAGGTATGTTAAACATTTCAACACCAATGCGTAAAAAACAATGTCCA
257▶nLeuGlnGlyMetLeuAsnIleSerGlnHisGlnCysValLysLysGlnCysPro
826 CAAAATTCGGATGTTTCAGACATTTAGATGAAAGAGAAGAAATGTAATGTTTAT
276▶GlnAsnSerGlyCysPheArgHisLeuAspGluArgGluGluCysLysCysLeuL
881 TAAATTACAAACAAGAAGGTGATAAATGTGTTGAAAATCCAAATCCTACTTGTA
294▶euAsnTyrLysGlnGluGlyAspLysCysValGluAsnProAsnProThrCysAs
936 CGAAAATAATGGTGGATGTGATGCAGATGCCAAATGTACCGAAGAAGATTCAGGT
312▶nGluAsnAsnGlyGlyCysAspAlaAspAlaLysCysThrGluGluAspSerGly
991 AGCAACGGAAAGAAAATCACATGTGAATGTACTAAACCTGATTCTTATCCACTTT
331▶SerAsnGlyLysLysIleThrCysGluCysThrLysProAspSerTyrProLeuP
PstII (1058)
1046 TCGATGGTATTTTCTGCAGTCACCACCACCACCACCTAACT
349▶heAspGlyIlePheCysSerHisHisHisHisHisHisHis...
```

Fig. 2

Codon	AA	MSP wt	Edited MSP	MSP wt	Edited MSP	E. coli	Human
TTT	Phe	8	0	0.53	0	0.5	0.35
TTC	Phe	7	15	0.47	0	0.5	0.65
TTA	Leu	25	0	0.66	0	0.11	0.05
TTG	Leu	3	0	0.08	0	0.11	0.09
TCT	Ser	4	1	0.17	0.04	0.21	0.26
TCC	Ser	2	3	0.09	0.13	0.21	0.26
TCA	Ser	10	1	0.43	0.04	0.13	0.11
TCG	Ser	0	0	0	0	0.14	0.07
TAT	Tyr	17	2	0.85	0.1	0.54	0.47
TAC	Tyr	3	18	0.15	0.9	0.46	0.53
TAA	***	0	0	0	0		
TAG	***	0	0	0	0		
TGT	Cys	10	12	0.83	1	0.45	0.3
TGC	Cys	2	6	0.17	0	0.55	0.7
TGA	***	0	0	0	0		
TGG	Tyr	0	0	0	0		
CTT	Leu	9	0	0.24	0	0.12	0.11
CTC	Leu	0	0	0	0	0.12	0.22
CTA	Leu	1	0	0.02	0	0.03	0.07
CTG	Leu	0	38	0.46	0	0.72	0.46
CCT	Pro	4	2	0.4	0.2	0.14	0.24
CCC	Pro	1	6	0.1	0.6	0.11	0.51
GCA	Pro	5	1	0.5	0.1	0.2	0.24
CGG	Pro	0	0	0	0	0.1	0.11
GAT	His	3	0	0.75	0	0.54	0.42
GAC	His	1	4	0.25	1	0.36	0.58
CAA	Gln	9	0	1	0	0.31	0.26
CAG	Gln	0	9	0	1	0.69	0.74
CGT	Arg	1	0	0.17	0	0.46	0.09
CGC	Arg	0	0	0	0	0.32	0.19
GGA	Arg	1	0	0.17	0	0.05	0.1
GGG	Arg	0	3	0	0.5	0.06	0.15
ATT	Ile	13	0	0.65	0	0.39	0.23
ATC	Ile	2	20	0.25	0	0.06	0.13
ATA	Ile	3	0	0	0	0.06	0.13
ATG	Met	3	3	1	1	1	1
ACT	Thr	3	2	0.19	0.13	0.36	0.2
ACA	Thr	3	13	0.19	0.81	0.38	0.47
ACG	Thr	9	1	0.56	0.06	0.03	0.21
ACG	Thr	1	0	0.06	0	0.17	0.12
AAT	Asn	29	3	0.71	0.07	0.29	0.14
AAC	Asn	12	38	0.29	0.93	0.71	0.66
AAA	Lys	38	0	0.9	0	0.72	0.45
AAG	Lys	4	42	0.1	0	0.28	0.55
AGT	Ser	5	2	0.21	0.09	0.11	0.11
AGC	Ser	2	16	0.09	0.7	0.14	0.29
AGA	Arg	4	3	0.67	0.5	0.08	0.24
AGG	Arg	0	0	0	0	0.03	0.23
GTT	Val	15	0	0.71	0	0.37	0.13
GTC	Val	1	11	0.05	0.52	0.12	0.27
GTA	Val	5	0	0.24	0	0.28	0.09
GTG	Val	0	10	0	0.48	0.23	0.5
GCT	Ala	2	0	0.22	0	0.33	0.11
GCC	Ala	1	8	0.11	0.89	0.18	0.4
GCA	Ala	6	1	0.62	0.11	0.28	0.17
CGG	Ala	0	0	0	0	0.21	0.12
GAT	Asp	25	27	0.93	0	0.48	0.36
GAC	Asp	2	0	0.07	0	0.52	0.62
GAA	Glu	21	3	0.84	0.12	0.67	0.4
GAG	Glu	4	22	0.16	0.88	0.33	0.6
GGT	Gly	8	4	0.57	0.29	0.46	0.15
GGC	Gly	0	0	0	0	0.4	0.44
GGA	Gly	6	3	0.43	0.21	0.05	0.17
GGG	Gly	0	7	0	0.5	0.08	0.24

Fig. 3b

Codon	AA	3b-casein	3b-casein	MSP wt	Edited MSP	mouse b-casein	mouse s-casein	mouse g-casein	mouse s-casein
TTT	Phe	5	4	8	4	0	8	3	4
TTC	Phe	4	3	7	15	4	6	7	1
TTA	Leu	0	2	25	0	0	0	0	0
TTG	Leu	0	2	3	0	0	0	0	1
TCT	Ser	5	1	4	13	0	5	7	5
TCC	Ser	2	2	2	3	6	14	8	2
TCA	Ser	1	4	10	1	1	3	2	0
TCG	Ser	0	1	0	0	0	0	2	0
TAT	Tyr	2	7	17	2	1	3	2	0
TAC	Tyr	1	2	3	18	2	6	6	7
TAA	***	1	2	0	0	1	1	1	0
TAG	***	0	0	0	0	0	0	0	0
TGT	Cys	1	0	10	12	0	0	1	0
TGC	Cys	0	2	2	0	2	2	2	1
TGA	***	0	0	0	0	0	1	1	0
TGG	Tyr	1	1	0	0	0	2	2	1
CTT	Leu	9	1	9	0	16	9	3	3
CTC	Leu	5	2	0	0	7	8	0	1
CTA	Leu	11	2	1	0	1	2	4	0
CTG	Leu	17	6	4	38	10	17	4	0
CCT	Pro	12	0	1	6	8	6	3	0
CCC	Pro	3	13	5	1	5	6	2	4
GCA	Pro	1	1	0	1	0	0	0	1
CGG	Pro	0	1	2	0	2	6	2	1
GAT	His	5	3	1	4	4	3	9	7
GAC	His	16	6	0	9	21	32	12	8
CAA	Gln	0	1	1	0	0	0	0	0
CAG	Gln	0	0	0	0	0	0	0	0
CGT	Arg	0	0	0	0	0	0	0	0
CGC	Arg	0	0	0	0	0	0	0	0
GGA	Arg	1	0	0	0	0	0	0	0
GGG	Arg	0	0	0	0	0	0	0	0
ATT	Ile	4	5	13	0	3	4	3	0
ATC	Ile	6	3	2	20	7	5	8	5
ATA	Ile	1	3	5	0	1	12	2	0
ATG	Met	7	3	3	2	4	5	1	13
ACT	Thr	2	6	3	6	6	4	1	4
ACA	Thr	2	4	9	1	1	4	4	4
ACG	Thr	0	0	1	0	0	0	2	0
AAT	Asn	2	6	29	3	4	6	3	1
AAC	Asn	2	3	12	38	4	9	4	6
AAA	Lys	7	6	38	0	6	7	3	5
AAG	Lys	6	4	4	42	3	6	6	7
AGT	Ser	2	6	5	2	3	6	5	5
AGC	Ser	5	0	2	16	2	6	6	3
AGA	Arg	2	2	4	3	1	8	1	1
AGG	Arg	0	2	0	0	0	0	0	0
GTT	Val	8	2	15	0	7	4	2	3
GTC	Val	2	1	11	0	7	3	3	0
GTA	Val	6	4	0	0	6	4	1	3
GTG	Val	1	3	2	0	8	3	5	2
GCT	Ala	4	7	1	8	6	17	4	3
GCC	Ala	3	7	6	1	4	13	1	1
GCA	Ala	0	1	0	0	0	0	0	0
CGG	Ala	4	5	25	27	3	6	4	2
GAT	Asp	0	2	2	0	1	2	1	3
GAC	Asp	10	6	21	3	6	12	5	8
GAA	Glu	9	5	4	22	5	5	3	5
GAG	Glu	2	1	8	0	0	0	0	0
GGT	Gly	0	0	0	0	0	0	0	0
GGC	Gly	2	1	6	3	1	0	1	0
GGA	Gly	1	0	0	0	0	0	0	0
GGG	Gly	0	0	0	0	0	0	0	0

Fig. 3a

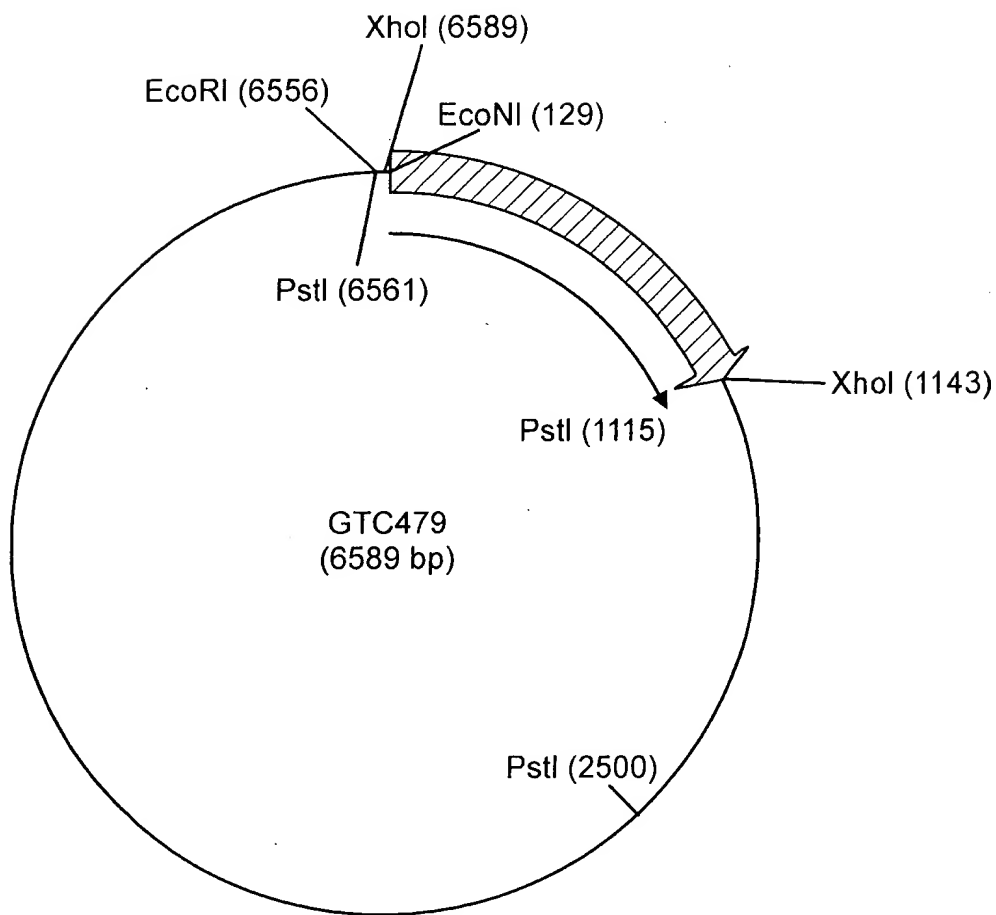


FIG. 4A

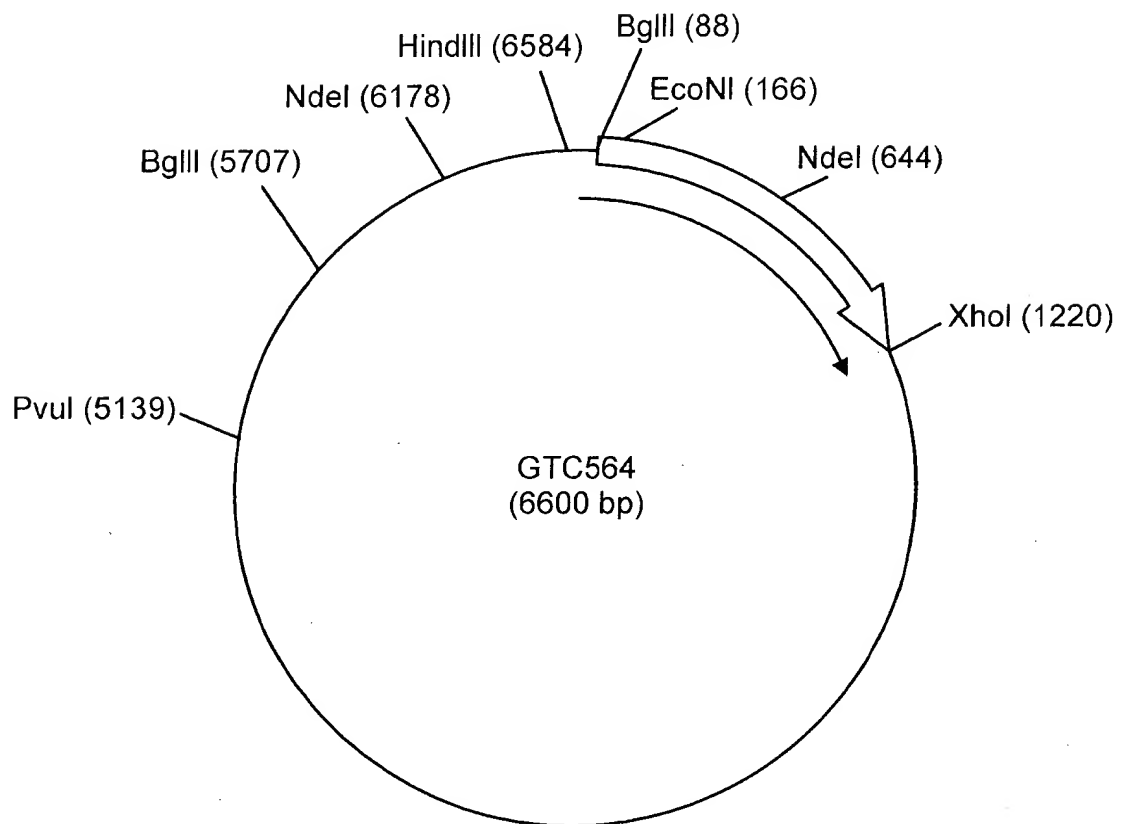


FIG. 4B

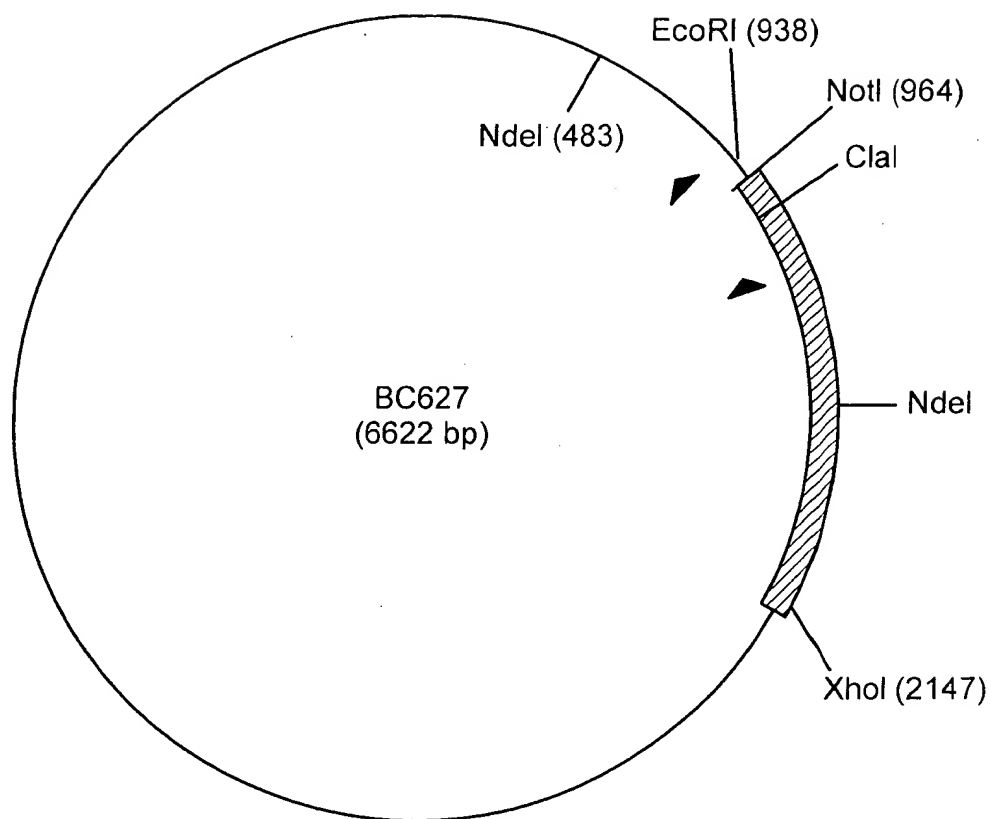


FIG. 4C

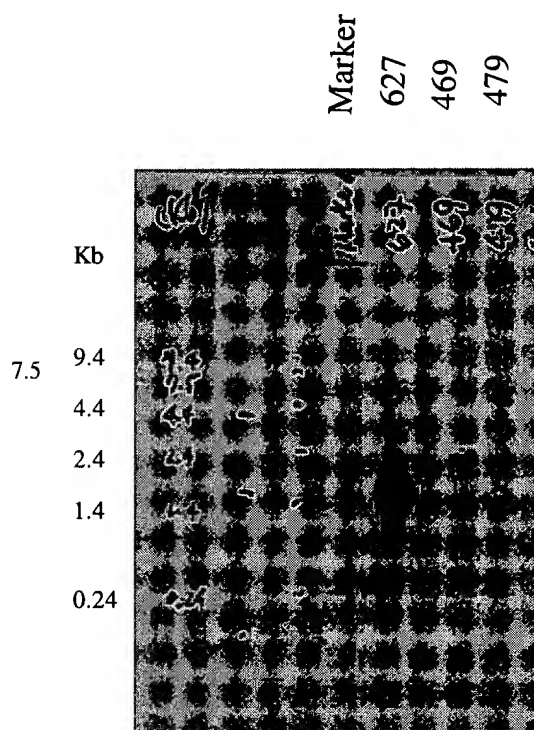


Fig. 5 Panel A

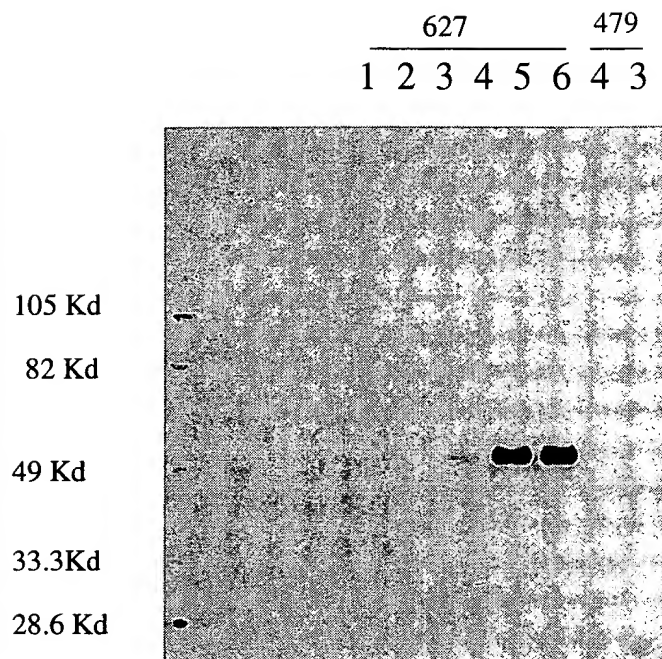


Fig. 5 Panel B

Oligos used:

Sequence ID NO. 3:
TCG ACG AGA GCC ATG AAG GTC CTC ATC CTT GCC TGT CTG GTG GCT
CTG GCC ATT GCA AGA GAG CAG GAA GAA CTC AAT GTA GTC GGT A,

Sequence ID NO. 4:
GAT CTA CCG ACT ACA TTG AGT TCT TCC TGC TCT CTT GCA ATG GCC
AGA GCC ACC AGA CAG GCA AGG ATG AGG ACC TTC ATG GCT CTC G,

Sequence ID NO. 5:
AATAGATCTGCAGTAACTCCTTCCGTAATTG,

Sequence ID NO. 6:
AATTCTCGAGTTAGTGGTGGTGCTGACTGCAGAAATACCATC

Sequence ID NO. J:
TAACTCGAGCGAACCATGAAGGTCCCTCATCCTTGCCCTGTGCTGGTCTG
CCATTGCA

FIG. 6

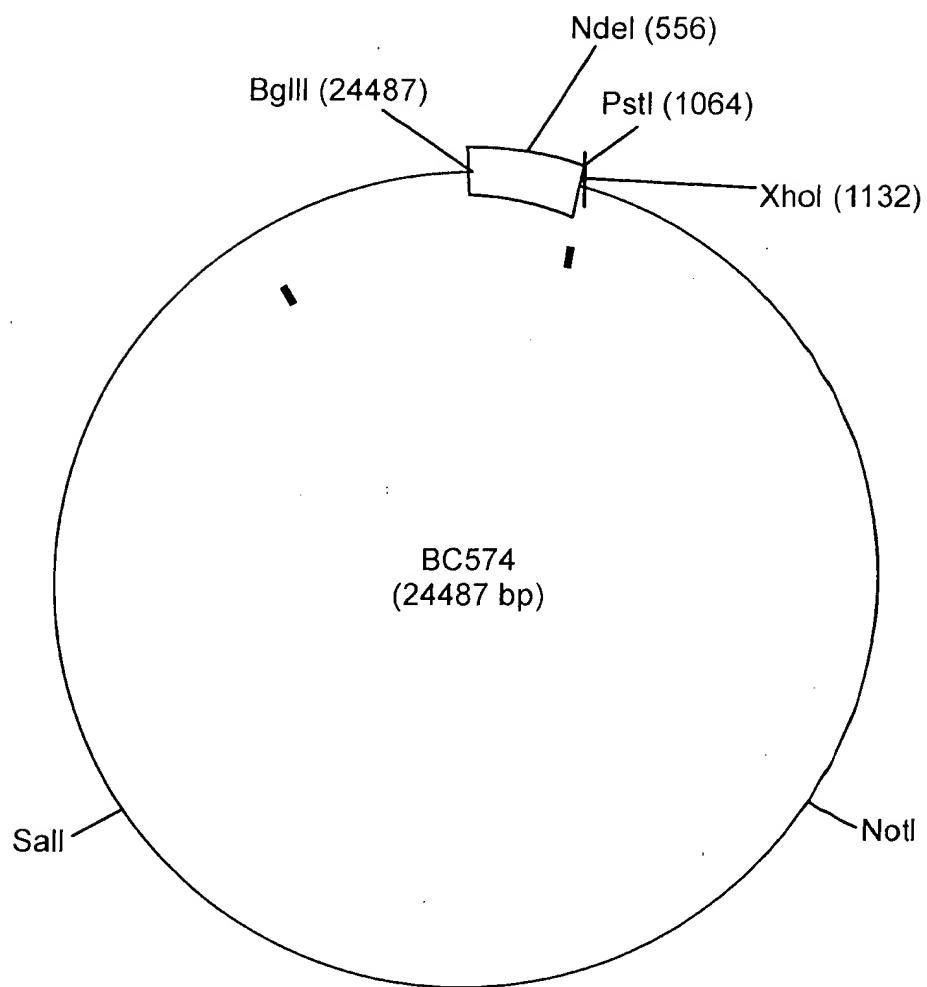


FIG. 7

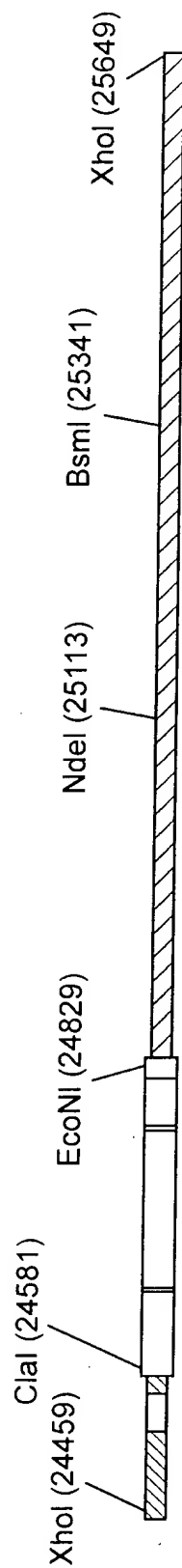


Diagram of BC620

FIG. 8

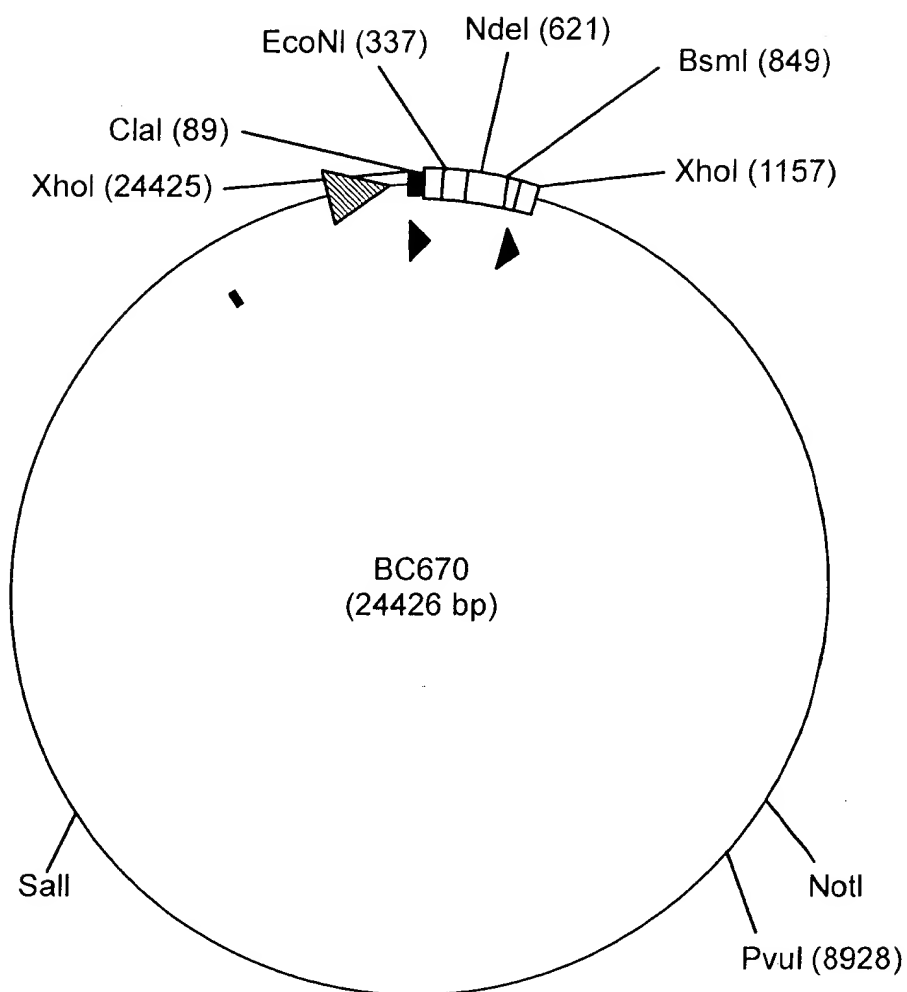


FIG. 9

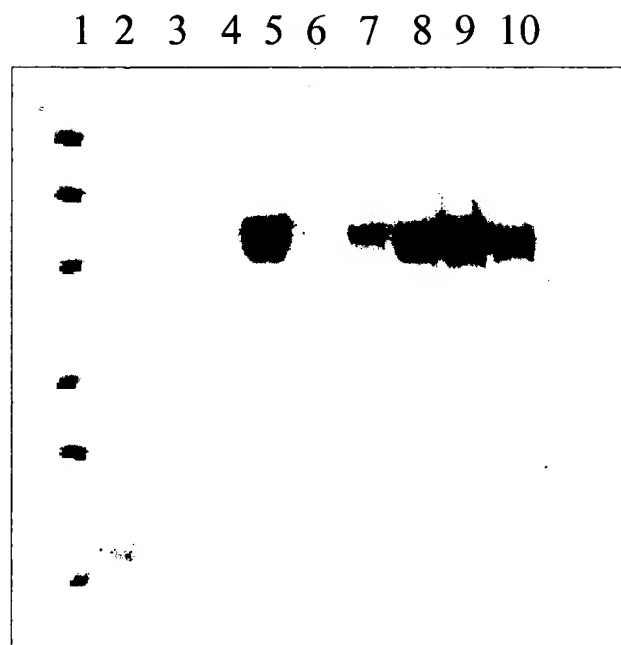


Fig. 10

26 CATGAAGGTCCTCATAATTCCTGTCTGTGGTGGCTCTGGCCATTGCGAGCGGTCACTCCCTCCGTCTCATCGATAA
1▶ M K V L I I A C L V A L A I A A V T P S V I D N
98 CATCTGTCCAAGATCGAAGACGAGTACGAGGTGCTGTACTCTGAAGCCCTGGCAGGAGTCTACAGGAGCC
24▶ I L S K I E N E Y E V L Y L K P L A G V Y R S
169 TGAAGAAGCAGCTGGCAACAACGTGATGACCTCAACCTGAACGTGAAGGATATCTCGAACACAGCGTTCA
48▶ L K K Q L E N N V M T F N V N V K D I L N S R F
241 ACAAGAGGGAGAAGTCAAGAACGTGTGGAGAGCGATCTGATCCCTACAAGGATCTGACCAGCAGCAACT
72▶ N K R E N F K N V L E S D L I P Y K D L T S S N
313 ACGTGGTCAAGAT AAGAGAGATAAGTTCTCTGAGCAGTTACAAATACA
96▶ V V K D P Y K F L N K E K R D K F L S S Y N Y
385 TCAAGGATAGCATTGACACCGGATCAACTTCGCCAACGATGTCTGGGATCTACAAGATCTCTGTCCGAGA
120▶ I K D S I D T D I N F A N D V L G Y Y K I L S E
457 AGTACAAGCGGATCTGGATAGCATCAAGAACTACATCAACGATAAGCAGGAGAGAGAACGAGAGTACCTGC
144▶ K Y K S D L D S I K K Y I N D K Q G E N E K Y L
529 CCTCTCTGAACACATCGAGACCCCTGTACAAGACCGTCAACGATAAGATTGATCTGTTCGTGATCCACCTGG
168▶ P F L N N I E T L Y K T V N D K I D L F V I H L
601 AGGCCAAG CAG A AGAGCAACGTGGAGGTCAAGATCAAGGAGCTGAATTACCTGA
192▶ E A K V L Q Y T Y E K S N V E V K I K E L N Y L
673 AGACCATCCAGGATAAGCTGGCCGATTTCAGAGAGAACACACACTTCGTGCGGAATCGCCGATCTGAGACCG
216▶ K T I Q D K L A D F K K N N N F V G I A D L S T
745 ATTACAACCAACAACCTCTGACCAAGTCTCTGAGCACCAGGAAATGGTCTTCGAAAACCTGGCCCAAGACCG
240▶ D Y N H N N L L T K F L S T G M V F E N L A K T
817 TCCTGAGCAACCTCTGGATGGAAACCTG CAG CAGCACCAGTGTGTGAAGAAG
264▶ V L S N L L D G N L Q G M L Q I S Q H Q C V K K
888 CAGTGTCCCCAGACAGCGGATGCTTCAGACACCTGGATGACAGGAGGAGTGCAGAGTGGCTGCTGAAGT
288▶ Q C P Q N S G C F R H L D E R E E C K C L L N
958 ACAAGCAGGAAGGAGATAAGTGTGTGGAACCCCACTCTTGTAAACGAGACAAATGGAGGATGCCAT
311▶ Y K Q E G D K C V E N P N P T C N E N N G C D
1029 GCCGATGCCAAGTCTACCGAGGAGGATTCAGGAAGCAACGAAAGAGATCACTCTGCGAGTGTACCAAGCC
335▶ A D A K C T E E D S G S N G K K I T C E C T K P
1100 TGATTCTTATCCACTGTTCGATGGATTTCTGAGTCACCAACCACCACCACTAACTCGAGGATCC
358▶ D S Y P L F D G I F C S H H H H H • L E D

Fig. 11

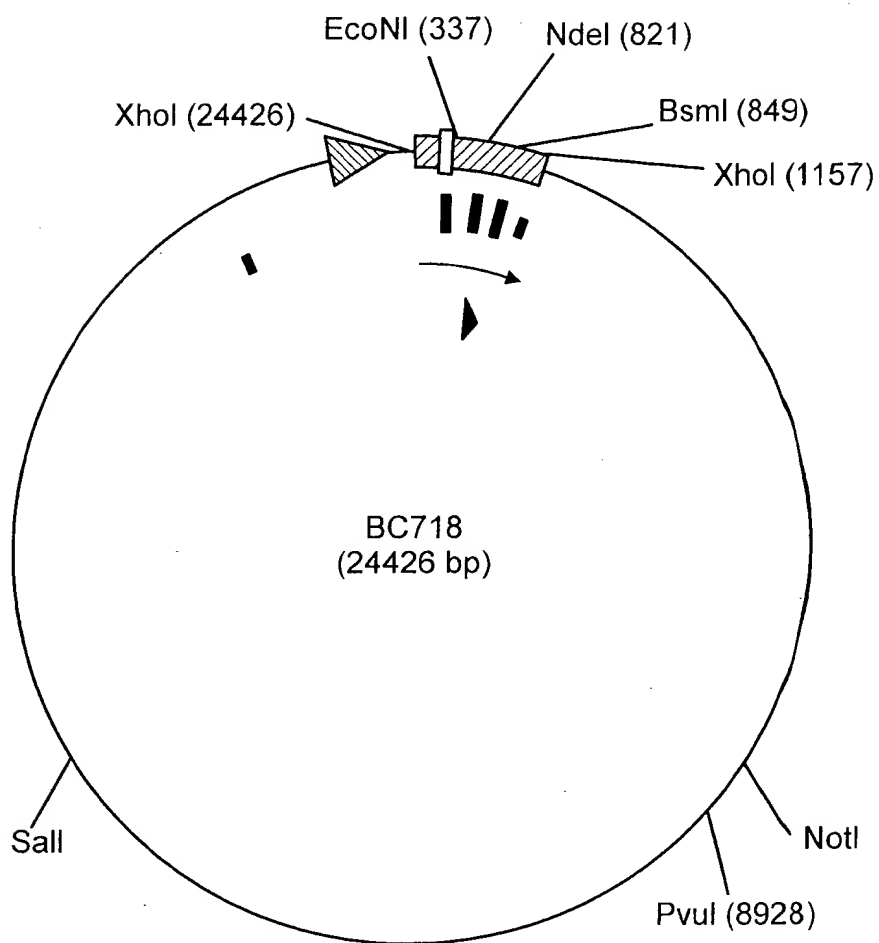


FIG. 12

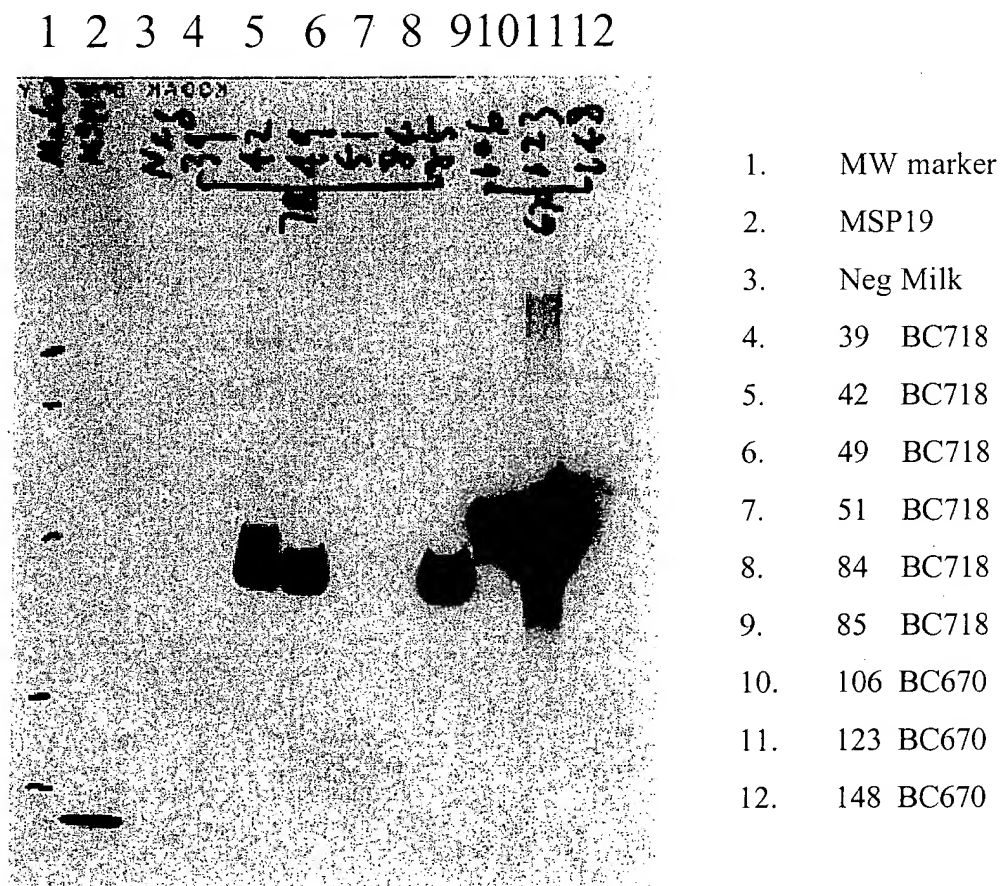


Fig. 13